

What is claimed:

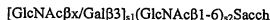
1. A pharmaceutical composition comprising a substance binding to a human tumor specific oligosaccharide sequence containing a terminal specifically protein linked
5 GlcNAc-structure, for the treatment of a human cancer.

2. The pharmaceutical composition according to claim 1, wherein said human cancer is a human tumor.

10 3. The pharmaceutical composition according to claim 1, wherein the composition is for the treatment of a human tumor diagnosed to express or compared to normal tissue expressing said human tumor specific oligosaccharide sequence.

4. The pharmaceutical composition according to claim 3, wherein said human tumor
15 specific oligosaccharide sequence is expressed on cell surface or tissue surface of human tumor.

5. The pharmaceutical composition according to any one of claims 1 – 4, wherein said oligosaccharide sequence has the sequence according to Formula
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wherein x is 3, when Sacch is Gal(NAc); or

x is 2, when Sacch is Man; and wherein

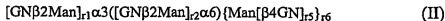
25 s1 and s2 are independently 0 or 1 with the provision that there is at least one terminal GlcNAc; the structure is branched, when both s1 and s2 are 1; Sacch is Gal with the provision that it is not $\alpha 6$ -linked to another GalNAc; Sacch is GlcNAc β with the provision that s1 and s2 is 0 and said GlcNAc β is linked to a protein or peptide; [GlcNAc β x/Gal β 3] means that terminal residue is either GlcNAc β x or Gal β 3.

30 6. The pharmaceutical composition according to any preceding claim, wherein said substance binding to said oligosaccharide sequence is specific to one or several of the terminal oligosaccharide sequences of a N-glycan type structure according to Formula



wherein r_1 , r_2 , r_3 , r_4 , r_5 , and r_6 are either 0 or 1 with the proviso that at least r_1 is 1 or r_2 is 1; GN is GlcNAc, with the proviso that when both r_1 and r_2 are 1, one GN β Man can be further elongated with one or several other monosaccharide residues such as by galactose, and/or one GN β 2Man can be truncated to Man, and/or Man α 6 residue and/or Man α 3 residues can be further substituted by GN β 6 or GN β 4, and/or Man β 4 can be further substituted by GN β 4.

7. The pharmaceutical composition according to any one of claims 1-5, wherein said substance binding to said oligosaccharide sequence is specific to one or several of the terminal oligosaccharide sequences of a N-glycan type structure according to Formula



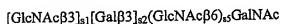
wherein r_1 , r_2 , r_5 , and r_6 are either 0 or 1, with the proviso that at least r_1 is 1 or r_2 is 1; GN is GlcNAc, with the proviso that when both r_1 and r_2 are 1, one GN β Man can be further elongated with one or several other monosaccharide residues such as by galactose, and/or one GN β 2Man can be truncated to Man, and/or Man α 6 residue and/or Man α 3 residues can be further substituted by GN β 6 or GN β 4, and/or Man β 4 can be further substituted by GN β 4.

8. The pharmaceutical composition according to claim 6, wherein said oligosaccharide sequence is

GlcNAc β 2Man, GlcNAc β 2Man α 3(GlcNAc β 2Man α 6)Man,
 GlcNAc β 2Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc,
 GlcNAc β 2Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc β 4GlcNAc,
 GlcNAc β 2Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc β 4(Fuc α 6)GlcNAc,
 GlcNAc β 2Man α 3(Man α 6)Man, GlcNAc β 2Man α 3(Man α 6)Man β 4GlcNAc,
 GlcNAc β 2Man α 3(Man α 6)Man β 4GlcNAc β 4GlcNAc,
 GlcNAc β 2Man α 3(Man α 6)Man β 4GlcNAc β 4(Fuc α 6)GlcNAc,

- Man α 3(GlcNAc β 2Man α 6)Man, Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc,
 Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc β 4GlcNAc,
 Man α 3(GlcNAc β 2Man α 6)Man β 4GlcNAc β 4(Fuca α 6)GlcNAc, GlcNAc β 2Man α 3Man,
 GlcNAc β 2Man α 3Man β 4GlcNAc, GlcNAc β 2Man α 3Man β 4GlcNAc β 4GlcNAc,
 5 GlcNAc β 2Man α 3Man β 4GlcNAc β 4(Fuca α 6)GlcNAc, GlcNAc β 2Man α 6Man,
 GlcNAc β 2Man α 6Man β 4GlcNAc, GlcNAc β 2Man α 6Man β 4GlcNAc β 4GlcNAc, or
 GlcNAc β 2Man α 6Man β 4GlcNAc β 4(Fuca α 6)GlcNAc

9. The pharmaceutical composition according to any one of claims 1-5, wherein said
 10 substance binding to said oligosaccharide sequence is specific to one or several of the
 terminal oligosaccharide sequences of a O-glycan type structure according to Formula



- 15 wherein s1, s2, s3, and s5 are independently 0 or 1, with the proviso that at least s1 is 1 or
 s5 is 1 and s3 is 1 or s5 is 1 and s3 is 1, so that the oligosaccharide sequence comprises at
 least one nonreducing end terminal GlcNAc β -residue.

10. The pharmaceutical composition according to any one of claims 1-5, wherein said
 20 oligosaccharide sequence is protein linked GlcNAc or a derivative thereof.

11. The pharmaceutical composition according to claim 9, wherein said oligosaccharide
 sequence is

- 25 GlcNAc β 3Gal β 3(Gal β 4GlcNAc β 6)GalNAc, GlcNAc β 3Gal β 3(GlcNAc β 6)GalNAc,
 GlcNAc β 3Gal β 3GalNAc, Gal β 3(GlcNAc β 6)GalNAc, GlcNAc β 3(GlcNAc β 6)GalNAc,
 GlcNAc β 6GalNAc, or GlcNAc β 3GalNAc

12. The pharmaceutical composition according to claim 3, wherein said substance binding
 30 to said oligosaccharide sequence is specific to one or several of the following terminal
 oligosaccharide sequences:

GlcNAc β 3Gal, GlcNAc β 3Gal β 4GlcNAc, GlcNAc β 6Gal, GlcNAc β 6Gal β 4GlcNAc
GlcNAc β 3(GlcNAc β 6)Gal, and GlcNAc β 3(GlcNAc β 6)Gal β 4GlcNAc

- said composition optionally further comprising at least one oligosaccharide sequences
5 defined in any one of claims 6-11, said composition being for the treatment of lung,
larynx, colon, gastric or ovarian cancer.
13. The pharmaceutical composition according to any preceding claim, wherein said
oligosaccharide sequence is not linked by natural glycosidic linkages to other
10 monosaccharide or oligosaccharide structures.
14. The pharmaceutical composition according to any preceding claim, wherein said
substance binding to said oligosaccharide sequence is an aptamer, a peptide or a protein.
- 15 15. The pharmaceutical composition according to claim 14, wherein said protein is an
antibody, a lectin, or a fragment thereof.
16. The pharmaceutical composition according to claim 14, wherein said protein is an
enzyme recognizing the terminal GlcNAc-structures, preferably a glycosyltransferase
20 enzyme or variant thereof.
17. The pharmaceutical composition according to claim 15, wherein said antibody is a
human or humanized antibody.
- 25 18. A pharmaceutical composition comprising a human tumor specific oligosaccharide
sequence containing a terminal beta-linked N-acetylglucosamine residue, GlcNAc β , or
analogous or derivatives thereof for the treatment of human lung, larynx, colon, gastric or
ovarian cancer.
- 30 19. The pharmaceutical composition according to claim 18, wherein said human cancer is
a human tumor.

20. The pharmaceutical composition according to claim 18, wherein the composition is for the treatment of a human tumor diagnosed to express or compared to normal tissue expressing said human tumor specific oligosaccharide sequence.
- 5 21. The pharmaceutical composition according to claim 18, wherein said human tumor specific oligosaccharide sequence is expressed on cell surface or tissue surface of human tumor.
22. The pharmaceutical composition according to claim 18, wherein said composition is
10 antigenic.
23. The pharmaceutical composition according to claim 18 or 19, wherein said oligosaccharide sequence is an oligosaccharide sequence as defined in any one of claims 1 and 5-12.
- 15 24. The pharmaceutical composition according to claim 23 comprising a polyvalent conjugate of said oligosaccharide sequence wherein position C1 of the reducing end terminal of the oligosaccharide sequence (OS) comprising the tumor specific terminal sequence of the invention is linked (—L—) to an oligovalent or a polyvalent carrier (Z), via
20 a spacer group (Y) and optionally via a monosaccharide or oligosaccharide residue (X), forming the following structure
- $$[\text{OS} - (\text{X})_n - \text{L} - \text{Y}]_m - \text{Z}$$
- 25 where integer m have values $m > 1$ and n is independently 0 or 1; L can be oxygen, nitrogen, sulfur or a carbon atom; X is preferably lactosyl-, galactosyl-, poly-N-acetyl-lactosaminyl, or part of an O-glycan or an N-glycan oligosaccharide sequence, Y is a spacer group or a terminal conjugate such as a ceramide lipid moiety or a linkage to Z.
- 30 25. The pharmaceutical composition according to any one of claims 1 - 24 comprising a pharmaceutically acceptable carrier and optionally an adjuvant.
26. A method for diagnosing cancer or tumor in a biological sample taken from a human patient, the method comprising determining the presence in said sample of an

oligosaccharide sequence which comprises a tumor specific terminal specifically protein linked beta-linked N-acetylglucosamine residue, GlcNAc β .

27. The method according to claim 26 wherein the determination comprises
- 5 (a) contacting said biological sample with a substance binding to said oligosaccharide sequence, and
- determining the presence of a combination of said substance and said sample, the presence of said combination being an indication of cancer present in said sample, or
- (b) releasing the oligosaccharide structures of said biological sample by enzymatic
- 10 or chemical methods to form a fraction containing free oligosaccharide structures from said sample, and
- determining the presence of said oligosaccharide sequence in said fraction, the presence of said oligosaccharide sequence in said fraction being an indication of cancer present in said sample.
- 15 28. The method according to claim 26 or 27, wherein said oligosaccharide sequence is a terminal oligosaccharide sequence as defined in any one of claims 1 and 5-12.
29. The method according to any one of claims 26-28, wherein said cancer is a tumor.
- 20 30. The method according to any one of claims 26-28, wherein a cancer or tumor type is determined.
31. The method according to any one of claims 26-30, wherein normal glycosylation of the
- 25 tissue containing the cancer is determined.
32. The method according to any one of claims 26-31, wherein the glycosylations are determined on the surface of cancer or normal tissue
- 30 33. Diagnostic agent comprising a binding substance as defined in any one of claims 1 – 17 for the diagnosis of human cancer or cancer type.
34. Antigenic substance comprising a terminal oligosaccharide sequence as defined in any one of claims 1 and 5-12 in a chemically or biochemically synthesized polyvalent form.

35. Use of the antigenic substance according to claim 34 or analogs or derivatives thereof to produce polyclonal or monoclonal antibodies.
- 5 36. Use of the antigenic substance according to claim 34 or analogs or derivatives thereof for the purification of antibodies from serum, preferably from human serum.
37. Use of the antigenic substance according to claim 34 or analogs or derivatives thereof for the detection and/or quantitation of antibodies.
- 10 38. A cancer vaccine comprising oligosaccharide sequences containing a terminal sequence as defined in any one of claims 1 and 5-12 or analogs or derivatives thereof.
39. The cancer vaccine according to claim 38 comprising a pharmaceutically acceptable
15 carrier and optionally an adjuvant.
40. A substance binding to oligosaccharide sequences containing a terminal sequence as defined in any one of claims 1 and 5-12, wherein said substance is an aptamer, human
20 natural or humanized antibody or peptide.
41. A method for identifying cancer or tumor specific therapeutics or diagnostic agents comprising the steps of contacting a compound with a oligosaccharide sequence as defined
in any one of claims 1 and 5-12 and determining binding to said oligosaccharide sequence
by said compound.
- 25 42. A human anti-GlcNAc antibody obtainable by:
passing human serum sample through a column containing immobilized terminal
GlcNAc β epitopes;
washing the column;
30 eluting the column with a buffer containing high concentration of GlcNAc;
and collecting the antibody.

43. A functional food or food additive containing antibodies recognizing tumor specific oligosaccharide sequences as defined in any one of claims 1 and 5-12 for the treatment of human cancer or tumor.
- 5 44. A functional food according to claim 41, wherein said antibody is produced in milk or in hen eggs.
45. The antibody according to claim 42, wherein said antibody recognizes oligosaccharide sequence $\text{GlcNAc}\beta 6\text{GalNAc}\alpha\text{-O-CH}_2\text{-R}$, $\text{GlcNAc}\beta 6(\text{Gal}\beta 3)\text{GalNAc}\alpha\text{-O-CH}_2\text{-R}$,
10 $\text{GlcNAc}\beta 2\text{Man}$ or $\text{GlcNAc}\beta\text{-O-CH}_2\text{-R}$ or $\text{GlcNAc}\beta 3\text{GalNAc}\alpha\text{-O-CH}_2$
46. Method of treatment or diagnosis of cancer or tumor comprising transferring a modified monosaccharide derivative to cancer cells or tumor by a glycosyl transferase or a transglycosylate enzyme.
- 15 47. The method according to claim 46 wherein said modified monosaccharide derivative is any type of terminal β -GlcNAc structures defined in any one of the preceding claims.
48. The method according to claim 46 wherein said modified monosaccharide derivative is
20 according to the formula
 $\text{UDP-GalN}[\text{-S}]\text{-D}$,
wherein
S is an optional spacer group
D is derivatizing group including molecular labels such as for example biotin or a
25 fluorescent molecule including, or a toxic agent, prodrug or prodrug releasing substance.
49. The method according to claim 48 wherein the modified monosaccharide is UDP-GalN-spacer-biotin or UDP- N-(6-biotinamidohexanoyl)galactosamine.
- 30 50. The method according to claim 46 wherein the modified monosaccharide is transferred by is a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or a natural GalNAc/GlcNAc-transferase with similar specificity with the said modified galactosyltransferase from animals.
- 35 51. The method according to claim 46 wherein said modified monosaccharide derivative is a non-immunogenic hydrophilic structure.

52. The method according to claim 46 wherein said modified monosaccharide derivative is transferred to cell or tissue.

53. The method according to claim 46 wherein said modified monosaccharide derivative is transferred on a therapeutic protein.

54. A substance according to

Formula P1:

Hex(L-S-PEG)-GlcNAc β -Core-peptide

10 wherein Hex, L and S are as described in Formula C1,

Core is a core structure of N-glycan and/or O-glycan, when GlcNAc is part of the core structure the core is the glycan core excluding a terminal GlcNAc residue, PEG is polyethylene glycol, and peptide is protein or peptide.

15 55. A substance according to

Formula CT2:

Gal(N-S-PEG)-GlcNAc β -Cell /tiss,

wherein S, PEG-core and peptide are as described in Formula C1.

20 56. Method of synthesis of substance according to claim 54 or 55 comprising transferring a modified monosaccharide by a modified galactosyltransferase.

57. A composition comprising an enzyme substrate, capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface, optionally conjugated to an immunologically active substance and/or a toxic substance for use as a medicine.

58. The composition according to claim 57, wherein said enzyme substrate is a carbohydrate substance capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme.

59. The composition according to claim 58, wherein said transferring enzyme is a glycosyl transferase or a transglycosylate enzyme.

35 60. The composition according to claim 57, wherein said carbohydrate substance is a nucleotide sugar.

61. The composition according to claim 60, wherein said nucleotide sugar is an activated salt of natural type of said nucleotide sugar.

62. The composition according to claim 60, wherein said nucleotide sugar is selected from the group consisting of:

UDP-Gal, GDP-Fuc, GDP-Man, UDP-GlcNAc, UDP-Glc, UDP-Xyl, UDP-GlcA and CMP-NeuNAc.

63. The composition according to claim 62, wherein the immunologically active substance or the toxic substance as defined in claim 57 is linked to carbon number 2 or 6 of the Gal, GalNAc, Glc or GlcNAc residues of UDP-Gal, UDP-GalNAc, UDP-Glc or UDP-GlcNAc, respectively.

64. The composition according to claim 62, wherein the immunologically active substance or the toxic substance as defined in claim 57 is linked to carbon number 6 of the Fuc residue of GDP-Fuc.

65. The composition according to claim 62, wherein the immunologically active substance or the toxic substance as defined in claim 57 is linked to carbon number 5, 7, 8 or 9 of CMP-NeuNAc.

66. The composition according to claim 62, wherein UDP-Gal is modified to carbon 6 by a spacer and a Gal α 3Gal-saccharide epitope.

67. The composition according to claim 58, wherein said carbohydrate substance is a glycoside being a substrate for a transglycosylase enzyme.

68. The composition according to claim 67, wherein said glycoside is phenyl- or paranitrophenylglycoside.

69. The composition according to claim 57, wherein said immunologically active substance is a carbohydrate or a carbohydrate analog or a derivative recognizable by immune system.

70. The composition according to claim 57, wherein said immunologically active substance is recognized by antibodies.

71. The composition according to claim 69, wherein said carbohydrate or a carbohydrate analog or a derivative comprises terminal GlcNAc β -, Gal α -antigen, or a blood group antigen.

72. The composition according to claim 71, wherein said blood group antigen is blood group A-antigen or blood group B-antigen.
73. The composition according to claim 57, wherein said immunologically active substance is recognized by a defensive cell surface receptor.
74. The composition according to claim 57, wherein said immunologically active substance is a carbohydrate recognized by non-antibody defense receptors of a patient.
75. The composition according to claim 57, wherein said immunologically active substance is a carbohydrate recognized by defensive lectins of the immune system of a patient or a terminal GlcNAc -recognising antibody substrate.
76. The composition according to claim 57, wherein said immunologically active substance is selected from the group consisting of:
- proteins, peptide antigens, non-harmful parts of peptidoglycan, non-natural epitopes, and lipid A of bacteria.
77. The composition according to claim 76, wherein the protein is a complement protein.
78. The composition according to any one of claims 57-77 further comprising a glycosyl transferase or a transglycosylating enzyme.
79. The composition according to claim 78, wherein said transglycosylating enzyme is a transsialidase.
80. The composition according to claim 78, wherein said glycosyl transferase is selected from the group consisting of:
- galactosyltransferases, N-acetylglucosaminyltransferases, N-acetylglactosaminyltransferases, fucosyltransferases, sialyltransferases, mannosyltransferases, xylosyltransferases, glucuronyltransferases and glucosyltransferases.
81. The composition according to claim 78, wherein said glycosyl transferase is selected from the group consisting of:

β 4galactosyltransferase, β 4glucosyltransferase, β 4-N-acetylglactosaminyltransferase, β 4-N-acetylglucosaminyltransferase, β 3galactosyltransferase, β 3-N-acetylglucosaminyltransferase, β 2-N-acetylglucosaminyltransferase, β 6-N-acetylglucosaminyltransferase, α 3sialyltransferase, α 6sialyltransferase, α 3fucosyltransferase, α 2fucosyltransferase and α 6fucosyltransferase.

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82. The composition according to claims 78, 80 or 81, wherein said glycosyltransferase is in soluble non-antigenic form.

83. The composition according to claim 57, wherein said pathogenic entity or malignant cell carries a specific carbohydrate structure on its surface, said structure being specifically recognised by said transferring enzyme.

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84. The composition according to claim 57, wherein said structure of said surface is a pathogenesis or metastasis -inducing carbohydrate receptor.

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85. The composition according to any one of claims 57 - 84 further comprising Mn^{2+} , Ca^{2+} , Zn^{2+} and/or Mg^{2+} ions.

86. The composition according to any one of claims 57 - 85 comprising the modified monosaccharide derivative as defined in any one of claims 46-53 and/or the substance as defined in claim 54 or 55.

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